CHEST

Lessons Learned

Risk Factors and Clinical Impact of Severe Pneumothorax After Endoscopic Lung Volume Reduction With Endobronchial Valves

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BACKGROUND: Pneumothorax is a major complication after endoscopic lung volume reduction with valves, with a prevalence of up to 34%. Although some patients benefit from valve implantation despite pneumothorax, others are significantly impaired after lung collapse.

RESEARCH QUESTION: What are the differences in the severity grades of pneumothorax and how do these affect clinical practice?

STUDY DESIGN AND METHODS: This single-center retrospective study analyzed patients undergoing endoscopic valve implantation with and without pneumothorax after intervention. Emphysema characteristics, collateral ventilation, management, and outcome of patients with pneumothorax 3 months after valve implantation were assessed. Pneumothorax was categorized as severe (chest tube insertion, prolonged air leak requiring valve removal), moderate (chest tube, no valve removal), and mild (no chest tube).

RESULTS: Pneumothorax occurred in 102 of 532 patients (19%) and was significantly more common after valve placement in the upper lobes (31.3%) compared with the lower lobes (11.3%; $P < .001$). Fissure integrity was significantly higher in patients with pneumothorax (mean, 96.6 $\pm$ 6.3% vs 93.4 $\pm$ 10.3%; $P = .002$). Of all pneumothoraces, 30.4% were mild, 30.4% were moderate, and 39.2% were severe. Severe pneumothorax caused multiple complications and prolonged hospitalization. Valve placement in the left upper lobe and a larger size of the target lobe were identified as risk factors for severe pneumothorax. Patients with pneumothorax demonstrated complete lobar atelectasis in $> 60\%$ as a sign of therapeutic success, but obviously only when valves could be left in place or reimplanted. However, valve reimplantation resulted in repeat pneumothorax in 42.9%.

INTERPRETATION: Patients could be informed more individually about their risk of pneumothorax, which varies with target lobe location, fissure integrity, and reimplantation. The poor outcome and high complication rate of severe pneumothorax calls for future research into the prediction of severe pneumothorax. CHEST 2025; 167(4):1012-1023

KEY WORDS: COPD; endobronchial valves; endoscopic lung volume reduction; pneumothorax; severe pneumothorax; valve removal

ABBREVIATIONS: DLCO = diffusion capacity of the lungs for carbon monoxide; EI = Emphysema Index; LUL = left upper lobe; mMRC = modified Medical Research Council

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Take-Home Points

Study Question: Can lessons still be learned from different severity grades of pneumothorax after endoscopic lung volume reduction with valves?

Results: The incidence of pneumothorax depends on the location of the target lobe and fissure integrity. Severe pneumothorax with valve removal is associated with a poor outcome, and valve reimplantation after valve removal for pneumothorax carries a high risk of repeat pneumothorax.

Interpretation: Patients need to be informed more individually about the risk of pneumothorax, and future research should focus on the prediction and prevention of severe pneumothorax.

Endoscopic lung volume reduction with endobronchial valves is an established treatment option for patients with advanced COPD, hyperinflation, and severe emphysema. It can improve lung function, exercise capacity, symptoms, quality of life,[1] and even survival.[2,3] However, endobronchial valve implantation also is associated with potential complications such as COPD exacerbation, hemoptysis, and valve dislocation.[4] Pneumothorax is one of the most common immediate complications of valve implantation.

The development of pneumothorax after valve implantation is complicated and different from other forms of pneumothorax. It usually develops as a result of rapid expansion of the adjacent lobe after complete atelectasis of the target lobe, which is associated with tension and tearing of the lung tissue or rupture of a bleb or bulla. Over the years, the pneumothorax rate has increased to 17.6% to 34.4% since the absence of collateral ventilation was identified as a key factor in the success of valve implantation and patients have been selected accordingly.[5] Several factors have been identified as predictive of pneumothorax, such as the Emphysema Index (EI) of the adjacent lobe, the size of the adjacent lobe in relationship to the hemithorax, the predominant type of emphysema,[6] and pleural adhesions,[7] or are highly suspected as risk factors, such as complete fissures, homogeneous emphysema, and rapid onset of lobar atelectasis.[5] Treatment pathways for the management of pneumothorax are already established, although some of the recommendations, such as the stepwise approach for valve removal for pneumothorax, are based on expert consensus, rather than evidence.[5]

The severity of a pneumothorax after intervention varies.[8] Pneumothorax ex vacuo describes a condition in which the acute collapse of the target lobe causes a sudden increase in negative intrapleural pressure, and gas and blood are drawn into the pleural space from the surrounding tissues.[5] These patients usually do not require a chest tube drainage and benefit greatly from the procedure. Pneumothorax after valve implantation in general was reported to have no negative effects on the survival of the patient.[9] The 4-year survival rate is even highest in patients with pneumothorax and complete lobar atelectasis (84.8%) compared with patients with complete lobar atelectasis without pneumothorax (73.1%).[2] However, severe forms of pneumothorax also can be accompanied by complete collapse of the lung and persistent air leak requiring further measures, such as valve removal, respiratory ventilation support, or surgical closure of the fistula in the case of a parenchyma leakage. Deaths after severe pneumothorax also have been reported.[10,11]

Clinical experience suggests that these patients with severe pneumothorax do not benefit from endobronchial valve implantation and even risk a worsening of the underlying disease. The aim of this study was to characterize different types of pneumothorax and their outcomes in a high-volume center for endoscopic lung volume reduction, paying particular attention to the event of severe pneumothorax.

Study Design and Methods

Study Overview

This study retrospectively analyzed all patients who underwent endobronchial valve implantation between January 2016 and May 2023 at a single center, specifically those who demonstrated pneumothorax in the first 3 months after the procedure. The diagnosis of pneumothorax was identified by International Classification of Diseases codes. The study was approved by the ethics committee of the Medical Faculty of Heidelberg (Identifier: S-621/2023) and was in accordance with the tenets of the Declaration of Helsinki in its current version. All patients gave written informed consent for the scientific use of their medical records.

Valve Implantation and Pneumothorax Management

Patient selection, endoscopic valve implantation, and management of pneumothorax were performed according to

best practice recommendations.[1,12] The details can be viewed in e-Appendix 1. We defined mild pneumothorax as pneumothorax without the need for chest tube drainage; moderate pneumothorax as pneumothorax with need for chest tube drainage, but with valves in situ; and severe pneumothorax as pneumothorax with chest tube drainage, prolonged air leak, and subsequent valve removal. In case of prolonged air leak, 1 or 2 valves were removed in clinically stable patients (ie, partial valve removal). If this did not lead to closure of the fistula, the remaining valves were removed in a second bronchoscopy (ie, sequential valve removal). In clinically unstable patients or those with large air leaks, all valves were removed immediately in 1 bronchoscopy (ie, immediate complete valve removal).

Data Collection

The following data were analyzed: EI and lung volumes (lung, hemithorax, contralateral hemithorax, target lobe, and adjacent lobe), obtained from the quantitative CT imaging software Yacta (in-house program of the University of Heidelberg) at 950 Hounsfield units[13]; fissure integrity (assessed by experienced radiologists); emphysema characteristics (paraseptal components, bullous emphysema, pleural adhesions, and others); perfusion scintigraphy; demographic data (age, sex, and former nicotine consumption in package years); BMI; lung function (FEV_1, residual volume, vital capacity, and total lung capacity, all in liters and percentage); diffusion capacity (diffusion capacity of the lungs for carbon monoxide [DLCO] and DLCO divided by the alveolar volume) in percentage; 6-minute walk distance; modified Medical Research Council (mMRC) dyspnea score; COPD Assessment Test results; extent and type of pneumothorax using radiography; multidetector CT imaging findings and clinical assessment (pneumothorax ex vacuo or interlobar pneumothorax, mantle or extensive pneumothorax, or tension pneumothorax); management of pneumothorax (chest tube insertion, second chest tube, valve removal, and surgical parenchymal fistula closure); and complications (subcutaneous emphysema, respiratory insufficiency [need of additional oxygen, high-flow oxygen therapy, noninvasive ventilation, and invasive ventilation], antibiotic therapy, cortisone therapy, hemoptysis, death, and tachyarrhythmia).

The primary outcome was the 90-day follow-up after valve implantation and, in the case of valve removal and subsequent reimplantation, 90 days after reimplantation of valves. Therefore, lung function, exercise capacity, symptom scores, and atelectasis rate (based on evaluation of multidetector CT scan findings: complete lobar atelectasis, lung volume reduction with partial atelectasis, no lung volume reduction) were assessed after 3 months.

Statistical Analysis

Statistical analysis was performed using IBM SPSS version 27 (IBM Corporation). Data are presented as mean ± SD or median (interquartile range). Frequencies are presented as absolute numbers and percentages. Data such as pneumothorax characteristics and management, as well as the reimplantation of valves, are presented only descriptively.

In the group of patients without pneumothorax, only target lobes, fissure integrity, and Chartis results were assessed. For patients with pneumothorax, all of the mentioned basic characteristics were analyzed. Patients with and without pneumothorax were compared for fissure integrity, target lobes, and Chartis (Pulmonx Corporation) results. Patients with and without valve removal and with partial vs complete valve removal were compared for all basic characteristics, collateral ventilation, emphysema characteristics, perfusion, quantitative CT scan findings, pneumothorax type, and complications. Comparisons were made by 2-sided Student *t* test for independent data or χ^2 test for frequency data. Data between 90-day follow-up and baseline were compared by 2-sided Student *t* test for paired data, separately for patients with mild or moderate pneumothorax, patients with valve removal and subsequent reimplantation, and patients with valve removal without subsequent reimplantation.

Because of the exploratory nature of the study, *P* values were interpreted descriptively. No adjustment was made for multiple testing. *P* values of $< .05$ were considered statistically significant.

Results

Patient Flow Chart and Occurrence of Pneumothorax

The patient flow chart is presented in Figure 1. Three patients were excluded from this analysis because of incomplete data (pneumothorax occurred in another hospital) or pneumothorax after valve removal because of poststenotic pneumonia (n = 2). The pneumothorax rate was 19% (102/532 patients).

The left lower lobe was the most common target lobe in the overall cohort of 532 patients (Table 1). The incidence of pneumothorax varied significantly for the

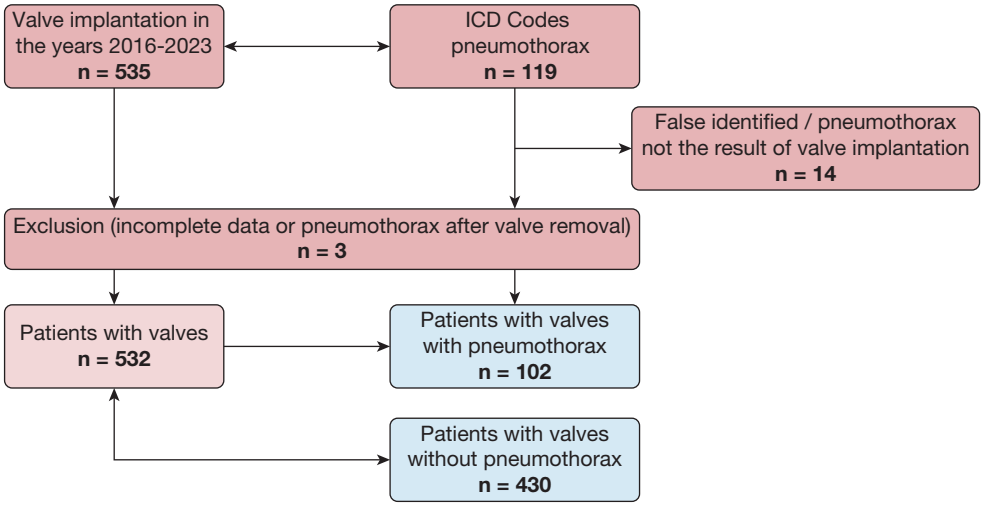

Figure 1 – *Flow diagram showing patient progression in the study. ICD = International Classification of Diseases.*

different target lobes, with a higher incidence after valve placement in the upper lobes (31.3%) compared with the lower lobes (11.3%; $P < .001$), even when assessing only patients with complete fissures of 95% to 100% ($P < .001$) (Fig 2).

The mean fissure integrity of 93.4 ± 10.3% (median, 95.0%; interquartile range, 90.0%-100.0%) in patients without pneumothorax was significantly lower compared with 96.6 ± 6.3% (median, 100.0%; interquartile range, 95.0%-100.0%) in patients with pneumothorax ($P = .002$). Patients with pneumothorax more frequently demonstrated complete fissures (80.4%) compared with patients without pneumothorax (64.7%; $P = .002$). Only 2 patients with a fissure integrity of < 95% and a target in one of the lower lobes demonstrated pneumothorax (vs 18 patients with fissure integrity of < 95% and target in the upper lobes).

TABLE 1] Target Lobes in the Basic Cohort of 532 Patients

Target Lobe(s)	No. (%)
RUL	67 (12.6)
RML	1 (0.2)
RUL plus RML	19 (3.6)
RLL	89 (16.7)
RLL plus RML	1 (0.2)
LUL	144 (27.1)
LLL	211 (39.7)

LLL = left lower lobe; LUL = left upper lobe; RLL = right lower lobe; RML = right middle lobe; RUL = right upper lobe.

Chartis measurement was performed in 128 patients; 15 of these patients (11.7%) demonstrated pneumothorax. Forty-four patients showed a low-flow phenotype in Chartis measurement, of whom 2 patients demonstrated pneumothorax (both in the upper lobes, and none in the lower lobes).

Pneumothorax Cohort and Characteristics

The following results refer to the 102 patients with pneumothorax whose basic characteristics are shown in

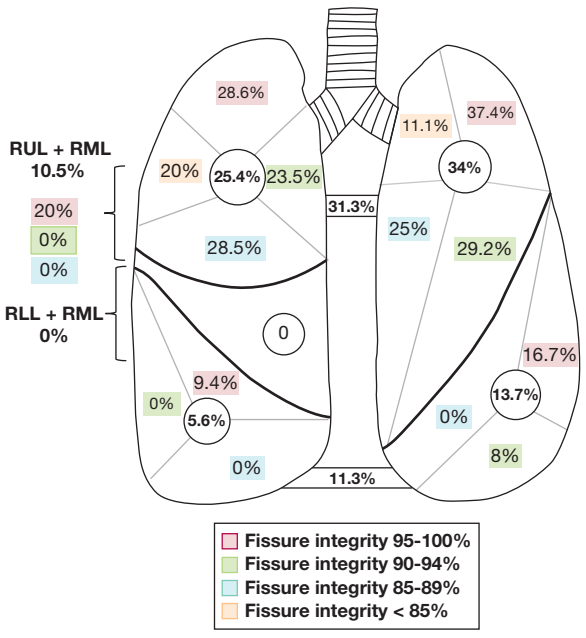

Figure 2 – *Diagram showing pneumothorax rate in different target lobes. RLL = right lower lobe; RML = right middle lobe; RUL = right upper lobe.*

Table 2. This cohort also includes severely ill patients with COPD with FEV_1 of < 20% (n = 11), DLCO of < 20% (n = 12), and 6-minute walk distance of < 100 m (n = 10). A proportion of 38.2% of all patients showed specific features of emphysema on multidetector CT imaging such as bullous emphysema, paraseptal distribution, or pleural adhesions, and 46.1% had heterogeneous emphysema with a mean target lobe EI of 48.0 ± 14.5%.

Most pneumothoraces (55.9%) occurred on the day of the procedure and 93.1% occurred within the first 3 days after valve implantation. In 4 patients, pneumothorax occurred only 5, 0, 5, and 49 days after a second bronchoscopy for valve replacement and reimplantation after previous removal.

Twenty-five patients (24.5%) demonstrated a tension pneumothorax. Chest tube drainage was required in 69.6% of all patients with pneumothorax (mean length of drainage, 9.0 ± 4.6 days) and 20.6% of all patients with pneumothorax required a second drainage (mean length of drainage, 9.9 ± 5.6 days). Subcutaneous emphysema was observed in 48.0% of all patients. The mean length of hospital stay was 13.0 ± 9.0 days (minimum, 3 days; maximum, 56 days; 33.3% of all patients stayed > 14 days in hospital), and a second hospital stay was required in 4 patients.

Respiratory failure developed in 41 patients (15 patients required high-flow oxygen therapy, noninvasive ventilation, or both; 4 patients required invasive ventilation). Twenty-two patients were transferred to intensive care, and surgical fistula closure was required in 9 patients. Further complications included hemoptysis, need for antibiotic therapy because of pneumonia, need for cortisone therapy because of COPD exacerbation, and tachyarrhythmia in 2.9%, 29.6%, 3.9%, and 3.9% of patients, respectively. One patient died as a result of multiorgan failure after surgical fistula closure with concomitant attempt for lung volume reduction and rupture of the left pulmonary artery.

Severe Pneumothorax and Valve Reimplantation

In total, 30.4%, 30.4%, and 39.2% of all patients demonstrated mild, moderate, and severe pneumothorax, respectively. No statistically significant differences for basic characteristics, such as lung function or emphysema characteristics, could be identified for patients with mild and moderate pneumothorax vs severe pneumothorax. Significant differences were noted regarding the target lobe for occurrence of severe pneumothorax, with the highest incidence (55.1%) after valve placement in the left upper lobe (LUL). Furthermore, the target lobe was significantly more hyperinflated in patients with severe pneumothorax (2002.3 ± 562.9 mL vs 1734.4 ± 603.5 mL; $P = .027$) (Table 2). Patients with severe pneumothorax underwent a longer hospital stay (18.3 ± 10.7 days vs 9.7 ± 7.0 days; $P < .001$) and more often demonstrated respiratory insufficiency (55% vs 30.6%; $P = .013$), subcutaneous emphysema (90% vs 21%; $P < .001$), and complications (hemoptysis; need for antibiotics, cortisone, or both; or tachyarrhythmia: 45% vs 21.0%; $P = .010$).

Valve removal was required in 40 patients. Two unusual cases of pneumothorax ex vacuo occurred that required chest tube placement and valve removal. One of these patients was discharged with pneumothorax ex vacuo, but a few days later, a chest tube was placed in an outside hospital, which worsened the patient's condition and led to valve removal in our hospital. A second patient with pneumothorax ex vacuo did not receive a chest tube, but valves were removed because progressive respiratory failure developed requiring noninvasive ventilation.

Partial valve removal was performed in 26 patients, but was sufficient in only 46.2% patients (12/26). The remaining patients underwent sequential complete removal of the remaining valves. In 14 patients, immediate complete valve removal was required. The rate of repeat pneumothorax overall was 42.9% and was higher in the cohort with sequential valve removal (75%) than in the group with partial valve removal (30%). In 3 patients, definitive complete valve removal was required after reimplantation and repeat pneumothorax (Fig 3).

Patients with partial valve removal showed significantly better DLCO (33.4 ± 9.3% vs 26.2 ± 9.4%; $P = .046$), better 6-minute walk distance (297.4 ± 92.6 m vs 216.0 ± 108.7 m; $P = .035$), and lower EI of the contralateral lung (30.3 ± 11.2% vs 39.7 ± 10.3%; $P = .014$) at baseline than patients with either sequential or immediate complete valve removal.

Endoscopic Lung Volume Reduction Outcome

At the 90-day follow-up, data were available for 74 patients (e-Appendix 2). The loss to follow-up rates were 9.7%, 21.4%, and 73.1% for patients with mild or moderate pneumothorax, severe pneumothorax with subsequent reimplantation, and severe pneumothorax without valve reimplantation, respectively.

TABLE 2] Basic Patient Characteristics and Comparison of Patients With Mild and Moderate vs Severe Pneumothorax

Variable	All Patients (n = 102)	Mild and Moderate Pneumothorax (n = 62)	Severe Pneumothorax (n = 40)	*P* Value
Demographics and baseline data				
Female sex	46 (45.1%)	32 (51.6%)	14 (35%)	.157
Age, y	63.4 (8.0)	62.9 (8.6)	64.2 (6.9)	.439
BMI, kg/m^2	23.7 (5.5)	23.7 (5.6)	23.7 (5.4)	.991
Nicotine consumption, pack-years	42.3 (20.8)	44.3 (20.9)	39.0 (20.5)	.210
Lung function and diffusion capacity				
FEV_1				
L	0.8 (0.2)	0.8 (0.2)	0.8 (0.3)	.759
%	28.7 (6.8)	28.6 (6.5)	28.8 (7.3)	.845
RV				
L	5.7 (1.3)	5.6 (1.4)	5.7 (1.2)	.900
%	254.2 (50.5	256.0 (47.8)	251.3 (55.2)	.654
VC				
L	2.4 (0.8)	2.3 (0.7)	2.5 (0.8)	.198
%	66.6 (17.0	65.7 (16.8)	67.9 (17.4)	.531
TLC				
L	8.1 (1.6)	8.0 (1.7)	8.2 (1.4)	.594
%	135.0 (17.9	135.4 (17.3)	134.3 (19.2)	.760
D_{LCO}, %				
D_{LCO} SB (n = 94)	30.1 (10.5)	31.3 (10.8)	28.1 (10.0)	.145
D_{LCO} Divided by VA (n = 95)	45.1 (14.4)	46.0 (13.8)	43.4 (15.5)	.406
Exercise capacity and symptoms				
6MWD (n = 92), m	251.1 (110.3)	261.4 (110.3)	236.4 (110.0)	.287
mMRC (n = 97), points	3.1 (1.0)	3.0 (1.1)	3.2 (0.8)	.353
CAT (n = 73), points	24.1 (7.4)	24.0 (6.7)	24.3 (6.7)	.879
Collateral ventilation				
Fissure integrity				
%	96.6 (6.3)	96.8 (6.7)	96.4 (5.5)	.377
95%-100%	13 (12.7%)	51 (82.3%)	31 (77.5%)	NS
90%-94%	3 (2.9%)	8 (12.9%)	5 (12.5%)	
85%-89%	4 (3.9%)	0 (0%)	3 (7.5%)	
< 85%	87 (85.3%)	3 (4.8%)	1 (2.5%)	
Chartis result				
CV negative	13 (12.7%)	9 (14.5%)	4 (10%)	.571
Low-flow phenomenon or collapse	2 (2%)	1 (1.6%)	1 (2.5%)	
Target lobe				**.019**
RUL	17 (16.7%)	12 (70.6%)	5 (29.4%)	
RML	0	0	0	
RUL plus RML	2 (2.0%)	1 (50%)	1 (50%)	

(Continued)

TABLE 2] *(Continued)*

Variable	All Patients (n = 102)	Mild and Moderate Pneumothorax (n = 62)	Severe Pneumothorax (n = 40)	*P* Value
RLL	5 (4.9%)	3 (60%)	2 (40%)	
LUL	49 (48.0%)	22 (44.9%)	27 (55.1%)	
LLL	29 (28.4%)	24 (82.8%)	5 (17.2%)	
Emphysema characteristics				NS
Paraseptal emphysema	15 (14.7%)	9 (14.5%)	6 (15%)	
Bullous emphysema	17 (16.7%)			
Target lobe	11 (10.8%)	7 (11.3%)	4 (10%)	
Adjacent lobe	6 (5.9%)	6 (9.7%)	1 (2.5%)	
Pleural adhesions	14 (13.7%)			
Target lobe	10 (9.8%)	9 (14.5%)	4 (10%)	
Adjacent lobe	4 (3.9%)	4 (6.5%)	1 (2.5%)	
Homogeneous emphysema	55 (53.9%)	35 (56.5%)	20 (50%)	.332
Perfusion score target lobe, %	8.01 (3.7) (n = 93)	8.4 (3.9) (n = 58)	7.3 (3.3) (n = 35)	.079
qCT imaging results, Yacta				
Lung				
EI, %	38.6 (10.9)	37.4 (11.3)	40.3 (9.9)	.188
Volume, mL	7,419.1 (1614.9)	7,312 (1648.7)	7,585.2 (1567.1)	.407
Hemithorax				
EI, %	41.9 (12.2)	40.7 (12.9)	43.7 (11.1)	.230
Volume, mL	3,658.0 (867.3)	3,587.2 (876.5)	3,767.8 (852.2)	.307
Contralateral hemithorax				
EI, %	35.1 (11.9)	34.0 (12.2)	36.9 (11.3)	.227
Volume, mL	3,781.3 (975.0)	3,704.8 (843.5)	3,900.0 (1151.1)	.326
Target lobe				
EI, %	48.0 (14.5)	46.6 (15.5)	50.1 (12.7)	.238
Volume, mL	1,839.5 (599.7)	1,734.4 (603.5)	2,002.3 (562.9)	**.027**
Adjacent lobe				
EI, %	35.5 (14.4)	35.4 (14.6)	35.8 (14.3)	.451
Volume, %	1,501.0 (635.2)	1,485.2 (641.5)	1,525.6 (632.7)	.378
Target lobe volume divided by lung volume	0.25 (0.05)	0.24 (0.05)	0.26 (0.05)	**.011**
Target lobe was not primary target	13 (12.7%)	8 (12.9%)	5 (12.5%)	.997
Pneumothorax type				
Tension pneumothorax	25 (24.5%)	7 (11.3%)	18 (45%)	**< .001**
Mantle or extensive pneumothorax	57 (55.9%)	38 (61.3%)	19 (47.5%)	
Pneumothorax ex vacuo or interlobar	20 (19.6%)	17 (27.4%)	3 (7.5%)	

Numbers are for n = 102 (all patients), n = 62 (mild and moderate pneumothorax), and n = 40 (severe pneumothorax) patients, unless otherwise indicated. Significant results appear in boldface. 6MWD = 6-minute walk distance; CAT = COPD Assessment Test; CV = collateral ventilation; D_{LCO} = diffusion capacity of the lungs for carbon monoxide; EI = emphysema index; LLL = left lower lobe; LUL = left upper lobe; mMRC = modified Medical Research Council; NS = not significant; qCT = quantitative CT; RLL = right lower lobe; RML = right middle lobe; RUL = right upper lobe; RV = residual volume; SB = single breath; TLC = total lung capacity; VA = alveolar volume; VC = vital capacity; Yacta = yet another CT scan analyzer.

Patients with mild or moderate pneumothorax experienced a statistically significant benefit in lung function (Table 3) with an atelectasis rate of 67.9%, as did patients with severe pneumothorax and subsequent valve reimplantation (66.7% atelectasis rate). Among patients with pneumothorax ex vacuo or interlobar pneumothorax

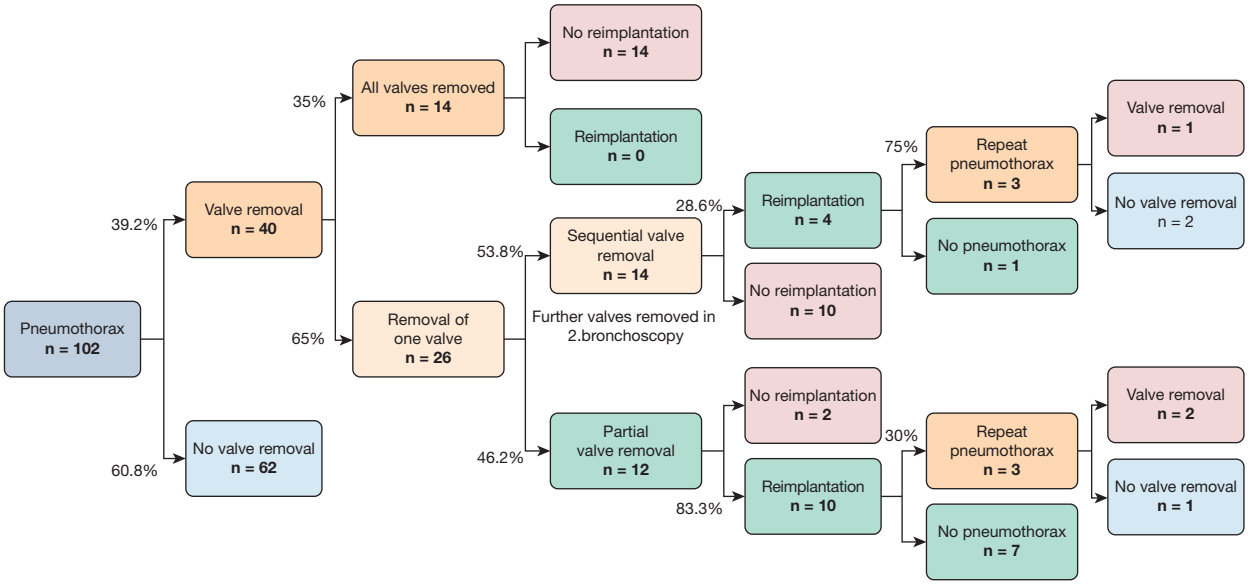

Figure 3 – *Diagram showing reimplantation of valves.*

(data available for 14 of 20 patients), 78.6% demonstrated complete lobar atelectasis. In total, 26 patients never underwent valve reimplantation. The patients without valve reimplantation experienced no statistically significant changes in lung function, exercise capacity, or symptom scores. Six of 102 patients subsequently were referred for lung volume reduction surgery.

Discussion

This retrospective analysis of 102 patients with pneumothorax after valve implantation revealed several findings. Pneumothorax was more likely to occur with intact fissures and after valve placement in the upper lobes, particularly in the LUL. A lower risk of pneumothorax was observed in patients with an upfront Chartis measurement, especially if the low-flow phenotype was observed. A stratification of pneumothorax by severity after occurrence seems to be useful, because patients with mild and moderate pneumothorax showed a high success rate of atelectasis, whereas the event of severe pneumothorax often was associated with complications and poor clinical outcome. In addition, valve reimplantation was associated with an increased risk of repeat pneumothorax.

The incidence of pneumothorax was significantly higher after valve placement in the upper lobes and highest after valve placement in the LUL in our study. The scientific community has been uncertain whether valve placement in the upper lobes is associated with an increased risk of pneumothorax.[5] Gompelmann et al[6] could not show that upper target lobes were a predictor of pneumothorax, but only patients with a complete lobar atelectasis were analyzed in this study. Two previous trials from 2015[14] and 2016[15] confirmed the increased incidence of pneumothorax after valve placement in the LUL (29.4% and 30.1%, respectively). This means that when the LUL is occluded with valves, the adjacent left lower lobe does not expand sufficiently and tears. This may be because occlusion of a large LUL, which has more segments with the lingula than the right upper lobe, exerts more traction on the left lower lobe during closure. However, this finding needs further investigation.

In contrast, the increased occurrence of pneumothorax in complete fissures (without the need for Chartis measurement) is expected. It is well known that the Chartis measurement is not a 100% reliable method for assessing collateral ventilation and that the low-flow phenotype is a false-negative finding in 30.2% of all measurements.[16] Therefore, it is reasonable to assume that pneumothorax is less common in intermediate fissures where Chartis measurement is required and collateral ventilation may still be present. This study cannot answer whether the relative absence of pneumothorax in patients with a Chartis measurement also indicates a lower treatment benefit of valve implantation, but this should be investigated in the future.

The severe pneumothorax rate of 39.2% in this study was higher than reported in previous studies

TABLE 3] Outcome 3 Months After Endoscopic Valve Implantation for Patients With Mild and Moderate Pneumothorax, Severe Pneumothorax, and Subsequent Valve Reimplantation and for Patients With Severe Pneumothorax Without Valve Reimplantation

Group	Parameters	No. of Patients With Available Data	Baseline	90-d Follow-up	*P* Value
Patients with mild and moderate pneumothorax (n = 62)	FEV_1				
	L	52	0.8 ± 0.3	0.9 ± 0.3	**< .001**
	%	51	28.7 ± 6.6	32.5 ± 9.5	**< .001**
	RV				
	L	51	5.5 ± 1.4	4.7 ± 1.3	**< .001**
	%	52	254.5 ± 50.2	213.3 ± 58.0	**< .001**
	VC				
	L	51	2.29 ± 0.67	2.36 ± 0.72	**< .001**
	%	51	69.63 ± 16.88	71.58 ± 19.13	**.002**
	TLC				
	L	51	7.9 ± 1.7	7.3 ± 1.6	**< .001**
	%	51	134.8 ± 18.1	123.5 ± 16.2	**< .001**
	D_{LCO}, %				
	D_{LCO} SB	45	31.0 ± 11.0	31.1 ± 10.3	.967
	D_{LCO} Divided by VA	45	46.0 ± 13.0	45.3 ± 13.7	.570
	mMRC	47	2.9 ± 1.2	2.7 ±1.2	.220
	CAT	35	24.2 ± 7.9	23.3 ± 7.5	.232
	6MWD, m	40	268.3 ± 92.4	288.5 ± 87.9	.139
	Complete lobar atelectasis	57	**67.9%** (38/56)	NA	NA
	LVR		23.2% (14/56)		
	No LVR		8.9% (5/56)		
Patients with severe pneumothorax and reimplantation of valves 3 mo later (n = 14)	FEV_1				
	L	11	0.9 ± 0.2	1.0 ± 0.3	.059
	%	11	27.9 ± 8.0	31.3 ± 13.2	.097
	RV				
	L	11	5.8 ± 1.0	5.2 ± 1.3	.094
	%	11	258.4 ± 41.8	231.6 ± 53.3	**.043**
	VC				
	L	11	2.8 ± 0.6	2.8 ± 0.9	.761
	%	11	72.9 ± 14.7	69.2 ± 18.6	.455
	TLC				
	L	11	8.6 ± 1.2	8.0 ± 1.4	**.024**
	%	11	137.1 ± 16.0	124.9 ± 12.7	**.015**
	D_{LCO}, %				
	D_{LCO} SB	9	32.4 ± 9.1	32.6 ± 7.4	.910
	D_{LCO} Divided by VA	10	49.5 ± 11.8	46.6 ± 17.9	.636

(Continued)

TABLE 3] *(Continued)*

Group	Parameters	No. of Patients With Available Data	Baseline	90-d Follow-up	*P* Value
	mMRC	8	3.3 ± 0.7	3.3 ± 0.7	1.000
	CAT	6	22.7 ± 6.0	23.3 ± 8.8	.847
	6MWD, m	10	298.3 ± 88.1	295.2 ± 71.5	.926
	Complete lobar atelectasis	12	**66.7%** (8/12)	NA	NA
	LVR		16.7% (2/12)		
	No LVR		16.7% (2/12)		
Patients with severe pneumothorax without valve reimplantation (n = 26)	FEV_1				
	L	7	0.8 ± 1.4	0.8 ± 1.3	.833
	%	7	24.8 ± 5.5	24.8 ± 4.6	.991
	RV				
	L	7	6.5 ± 1.2	6.1 ± 1.1	.260
	%	7	272.4 ± 51.7	253.2 ± 38.2	.216
	VC				
	L	7	2.4 ± 0.7	2.4 ± 0.5	.877
	%	7	59.0 ± 17.2	60.4 ± 13.4	.764
	TLC				
	L	7	8.9 ± 0.9	8.5 ± 1.1	.099
	%	7	134.7 ± 11.5	129.1 ± 11.5	.080
	D_{LCO}, %				
	D_{LCO} SB	7	18.8 ± 4.8	22.5 ± 5.4	.200
	D_{LCO} Divided by VA	7	31.7 ± 9.2	36.3 ± 6.5	.291
	mMRC	6	3.5 ± 0.8	3.0 ±1.3	.363
	CAT	4	22.5 ± 7.5	24.3 ± 8.5	.562
	6MWD, m	5	216.2 ± 62.5	299.6 ± 63.8	.092
	Complete lobar atelectasis	7	**0** (0/7)	NA	NA
	LVR		14.3% (1/7)		
	No LVR		85.7% (6/7)		

Data are presented as No. or mean ± SD. Statistically significant results appear in boldface. 6MWD = 6-minute walk distance; CAT = COPD Assessment Test; D_{LCO} = diffusion capacity of the lungs for carbon monoxide; LVR = lung volume reduction; mMRC = modified Medical Research Council; NA = not applicable; RV = residual volume; SB = single breath; TLC = total lung capacity; VA = alveolar volume; VC = vital capacity.

(ie, 0%-11.6%),[5] most probably because of improved patient selection with a higher rate of complete fissures. Patients with severe pneumothorax had multiple complications and showed no long-term benefit from therapy; 1 patient even died. Whether their clinical condition and lung function may even deteriorate cannot be answered from our study, because many patients did not return for follow-up after valve removal. It is clear that only those patients with pneumothorax who keep their valves (or have them reimplanted) benefit. A high atelectasis rate was observed in these patients. This is in line with data from Gompelmann et al,[2] who showed that the 4-year survival rate was highest in patients with complete lobar atelectasis and pneumothorax (84.8%) compared with patients with complete lobar atelectasis without pneumothorax (73.1%), patients without atelectasis or pneumothorax (60.1%), and patients with pneumothorax without concomitant atelectasis (54.4%).

Our study identified the size of the hyperinflated target lobe and valve placement in the LUL as potential risk

factors for the development of severe pneumothorax. In contrast, the Pulmonx Endobronchial Valves Used in Treatment of Emphysema (LIBERATE) study[11] showed that patients were at higher risk of so-called complex pneumothorax (defined as death or complete valve removal) if the lobe with the highest destruction score was not treated and the EI of the untreated contralateral lung was > 60% (EI measured at –910 Hounsfield units).

To our knowledge, this is the first study to provide detailed data on the risk of repeat pneumothorax after valve reimplantation. Recurrence rates of 17% and 29% have been reported from 2 centers without details.[5] Valve reimplantation after removal for pneumothorax was associated with an increased risk of repeat pneumothorax in this cohort, especially when all valves had to be removed (75% risk of repeat pneumothorax). The decision for valve reimplantation therefore should be discussed critically with the patient, although it is difficult to derive clinical recommendations from these few retrospective data.

The main limitation of this study is its retrospective nature. It represents a reflection of clinical practice, which is already adapted to expert consensus guidelines[5] and clinical experience with pneumothorax. A prospective evaluation of pneumothorax incidence and other specific clinical scenarios in patients with a high risk of pneumothorax developing after valve (re)implantation (eg, those with bullous or paraseptal emphysema or those with complete immediate valve removal) in a randomized controlled study has severe ethical restrictions. Therefore, observational studies must continue to be conducted and used to verify previous assumptions about the development of pneumothorax. Another weakness of the study is that the basic cohort of all patients with valve implantation has not been characterized fully. Therefore, it is not possible to reliably predict (severe) pneumothorax from this study and to make further comparisons between patients with and without pneumothorax. The analysis of fissure integrity was carried out by experienced radiologists and not by quantitative CT imaging in our study. This may have limitations in the informative value of the fissure integrity, even if the results seem reliable.

In the future, studies including large cohorts with and without severe pneumothorax after valve implantation should come closer to predicting severe pneumothorax. Something like a score that can predict the occurrence of pneumothorax better, especially severe pneumothorax, and that can be used in daily clinical practice, certainly would be helpful. Studies on the prevention of pneumothorax, such as the sequential valve implantation approach,[17] should concentrate on severe forms of pneumothorax in terms of cost-benefit analysis, because the prevention of mild pneumothoraces without the need for further invasive measures and with a good outcome does not seem to be necessary.

Interpretation

The data presented allow for a more accurate assessment of pneumothorax risk and for patients to be informed more individually about the expected risk of (severe) pneumothorax depending on the target lobe and fissure integrity. A categorization of the severity of pneumothorax, and in particular a distinction between severe pneumothorax and mild or moderate pneumothorax, seems to be useful for further studies and reporting, because severe pneumothorax is an enormous burden for the patient and is not associated with the same therapeutic success as mild and moderate pneumothorax. The possibility of valve reimplantation after complete valve removal resulting from severe pneumothorax should be discussed critically with the patient, because the risk of repeat pneumothorax is high. Although valve implantation has become a routine procedure in many hospitals, the complications of this procedure still need to be considered. Future research should focus on the prediction and prevention of severe forms of pneumothorax.

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